

Postgonococcal urethritis

Relationship to penicillin sensitivity of the gonococcus

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SUMMARY Postgonococcal urethritis (PGU) occurred in 69 (21.3%) of 344 men with urethral gonorrhoea. Each case of gonorrhoea was treated with intramuscular procaine penicillin 2.4 megaunits and the penicillin sensitivity was determined. All 69 of the isolates from patients with PGU were fully sensitive to penicillin ($IC_{50} < 0.08$ iu penicillin per ml). Twenty-eight (10.2%) of 275 cases of gonorrhoea which were not followed by PGU were relatively resistant to penicillin. The persistence of gonococcal L-forms is therefore not likely to be a main cause of PGU. An incidental finding was that significantly more of the 69 men who developed PGU had a history of non-specific urethritis compared with the 224 men who fully recovered ($P < 0.01$).

Introduction

In a study that described a direct immunofluorescent test for identifying gonococcal L-forms, the possibility that these organisms were responsible for postgonococcal urethritis (PGU) was raised (Waitkins and Geary, 1977). L-forms may be induced by relatively low concentrations of penicillin (Lawson and Douglas, 1973) and their presence in urethral secretions of those suffering from gonorrhoea has been reported (Gnarpe *et al.*, 1972). The higher incidence of PGU after treatment with penicillin, compared with tetracycline (which does not induce L-forms), favours this hypothesis (Holmes *et al.*, 1967). Holmes *et al.* (1967) studied 49 patients treated with penicillin; the penicillin sensitivity was determined and PGU was more common after gonococcal infection caused by less sensitive organisms.

In the present study a retrospective analysis was made of the incidence of PGU related to the penicillin sensitivity of the gonococcus. This study was on a much larger group of patients, all of whom received intramuscular procaine penicillin 2.4 megaunits for urethral gonorrhoea. A statistical analysis of the results is given.

Patients and methods

The study period was from 1 May to 31 December 1976. Three hundred and forty-four consecutive

cases of urethral gonorrhoea, in 293 individuals, in whom the penicillin sensitivity of the causative gonococcus had been determined, were analysed. The initial treatment of each infection was intramuscular aqueous procaine penicillin 2.4 megaunits. The diagnosis of urethral gonorrhoea was made if Gram-negative diplococci were found on a stained smear of urethral discharge or scraping and if it was confirmed by positive results to culture of the organism, including sugar fermentation and/or fluorescent antibody tests.

The penicillin sensitivity of subcultures was determined using a plate dilution method (Reyn *et al.*, 1963). The results obtained were expressed as 50% inhibitory concentration (IC_{50}), and were standardised using reference strains from the State Serum Institute, Copenhagen. Cultures with IC_{50} greater than 0.08 iu penicillin per ml were regarded as relatively resistant.

If gonococci still persisted in the urethral smear or on urethral culture within one week of treatment, the treatment was regarded as having failed. The diagnosis of PGU was made in those who had a persistent purulent or mucopurulent urethral discharge seven days after treatment of the initial infection, or in whom a discharge reappeared within 28 days of primary treatment. Specimens of urethral secretion were taken with a wire loop after urethral massage. Gram-stained smears and a wet film for trichomonads were prepared. The finding of eight or more leucocytes per field using a $\times 100$ oil immersion objective together with negative findings for gonococci and trichomonads by smear and culture, was considered diagnostic of non-specific

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urethritis. In addition all patients had pus in the urine manifest as haze, flocculations, or threads in one or both glasses.

Yates's χ^2 test was used for statistical calculations.

Results

PGU was diagnosed in 69 (21.3%) of the 344 infections. These 69 men constituted the postgonococcal urethritis group (PGU Group) and were compared with 224 men who had no evidence of persisting urethral discharge—the gonorrhoea only group (GO Group). Thirty-seven (12.6%) men, all in the GO Group, had more than one gonococcal infection. Mean age, country of origin, and marital state were similar in both groups (Table 1). Fifteen (21.7%) of 69 patients in the PGU Group compared with 67 (29.9%) of 224 patients in the GO Group had had gonorrhoea previously. This difference was not significant ($P > 0.1$). Only a few patients in both groups had a history of trichomoniasis. There was,

however, a significant difference in the incidence of patients with a history of non-specific urethritis ($P < 0.01$). Such a history was present in 20 (29%) of 69 patients in the PGU Group, but only in 30 (13.4%) of 224 patients in the GO Group.

The gonococci isolated in all 69 infections in the PGU Group showed an IC_{50} less than 0.08 iu of penicillin per ml—that is, they were sensitive strains. In the GO Group 28 (10.2%) of 275 infections were caused by organisms which were relatively resistant to penicillin; all organisms showed an IC_{50} greater than 0.1 iu penicillin per ml. Two hundred and forty-seven (89.8%) of the 275 strains were sensitive. The difference between the two groups was significant ($P < 0.02$), Table 2.

There were six treatment failures in the GO Group owing to relatively resistant organisms. Secondary treatment of three patients with kanamycin 2 g intramuscularly and three with spectinomycin 2 g intramuscularly was successful. After initial treatment with penicillin no treatment failure was diagnosed in any infection due to a sensitive organism in either group.

Table 1 History and details of patients

Postgonococcal urethritis (no. of infections 69; no. of individuals 69)		Gonococcal urethritis only (no. of infections 275; no. of individuals 224)	
No.	%	No.	%
Age groups			
Younger than 16 years			
—	—	1	0.4
16–19	18	38	17.0
20–24	26	71	31.7
25–34	20	85	37.9
35–44	3	20	8.9
45 and over	2	9	3.8
Mean \pm SD	24.82 \pm 6.88	26.54 \pm 7.40	
Country of origin			
UK	49	168	75.0
West Indies	14	36	16.1
Europe	—	4	1.8
Africa	—	4	1.8
Middle East	5	5	2.2
Pakistan	1	6	2.7
South America	—	1	0.4
Marital state			
Single	48	145	64.7
Married	15	56	25.0
Separated	3	13	5.8
Divorced	3	10	4.5
History			
Gonorrhoea	15	67	29.9
Non-specific genital infection	20	30	13.4
Trichomoniasis	2	6	2.7

*Difference by Yates's χ^2 test $\chi^2 = 1.37$

At one degree of freedom $P > 0.1$

†Difference by Yates's χ^2 test $\chi^2 = 7.99$

At one degree of freedom $0.01 > P > 0.005$

Table 2 Sensitivity of strains

	PGU group		GO group	
	No.	(%)	No.	(%)
No. of infections in which IC_{50} was determined	69		275	
$IC_{50} > 0.08$ iu penicillin per ml	—		28	(10.2)
$IC_{50} < 0.08$ iu penicillin per ml	69	(100)	247	(89.8)

$\chi^2 = 6.35$ (using Yates's modification)

At one degree of freedom $0.02 > P > 0.01$

Discussion

If gonococcal L-forms, whose formation may be induced by relatively low penicillin concentrations, are a main cause of PGU, it would be expected that a greater proportion of infections caused by gonococci that are relatively resistant to penicillin would be followed by this condition as reported by Holmes *et al.* (1967). The results reported here contrast with those obtained by Holmes *et al.* (1967). An unexpected finding was that all cases of PGU followed gonococcal infections that were fully sensitive to penicillin. If an infective agent is the cause of PGU it is likely to be other than the gonococcal L-form. The PGU Group and GO Group differed in the proportion of patients with a history of non-specific urethritis. Other differences that were not assessed but which may be important are contraceptive methods, alcohol intake, and sexual behaviour.

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